PHILIP MORRIS INCORPORATED

LAW DEPARTMENT MEMORANDUM

RICHMOND, VIRGINIA

(F)

CPF

TO: T. Osdene DATE: April 11, 1983

FROM: G. Inskeep

SUBJECT: OPTICALLY ACTIVE NICOTINE ANALOGS AND PROCESS FOR THEIR PREPARATION/USSN 377,989/PM 893 DIV II

For your information, we attach a copy of the Official Action recently received in this case.

If you have any comments to offer before we begin preparation of a response, please let me know. We prefer not to have you or the inventor(s) write anything at this stage about the Action or the invention, or go to any trouble interpreting or analyzing the Action. At the appropriate time, we will arrange to get from the inventor(s) anything needed to help us in preparing a response.

On the other hand, if it should appear to you that the case might not be worth pursuing, please call to give me your views on that aspect.

bjm

cc: W. Edwards, III
E. Sanders
S. Hutcheson

Les

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Source: https://www.industrydocuments.ucsf.edu/docs/pbj0000

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 48, 50 and 54 are rejected under 35 U.S.C. 102a as being anticipated by Morrin et al..

Specifially, the Morrin et al. article abstracted by Chemical abstracts, Vol. 93, No. 13 #132,669-e dated Sept. 29, 1980 discloses the compounds 1,4,4-trimethyl-2-(3-pyridyl)-2-pyrrolidinone and the reduced form, namely, 1,4,4-2(3-pyridyl)-2-pyrrolidine as well as ,4-dimethyl-2-(3-pyridyl) -pyrrolidine, methods for their preparation; said compounds clearly read on the instant claims.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

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A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 49, 51-53 and 55 are rejected under 35 U.S.C. 103 as being unpatentable over Morrin et al. and march.

Specifically, the Morrin et al. article abstracted by Chem. Abstracts, has been discussed above and to reiterate, the (S) or Sinister absolute configuarations of the 3 above cited compounds are the optically active counterparts of claims 49, 51-53 and 55 which are in the (R) or Rectus absolute configuration or in the form of the mixed diastereomers. The March textbook teaches in Pages 108-111, the several known methods for Resolution into either the Sinister or Rectus absolute configuarations or the mixed diastereomers as well as well as the concept of optical purity, raising a presumption of obviousness.

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Source: https://www.industrydocuments.ucsf.edu/docs/qbbj0000

Claims 44-47 are rejected under 35 U.S.C. 103 as being unpatentable over hecht et al. and March.

Specifically, the Hecht et al. article appearing in Journal of Medicinal Chemistry, Vol 23, Pages 1175-78(1980) discloses the Synthesis of 4'-hydroxy-nornicotine which differs form the claimed compounds by being devoid of the N-methyl moiety being attached to the pyrrolidine ring. The March textbook again teaches methods for Resolution and the concept of optical purity. The combination of references raises a presumption of obviousness.

Claims 40-43 are rejected under 35 U.S.C. 103 as being unpatentable over Castonguay et al. and March.

Castonguay et al. reference appearing in J. of Org. Chem., Vol. 44, No. 23, Pages 4332-37(1979) discloses in page 4332, compound No. 16 which is a position isomer of the claimed compounds. Note in page of 4334, synthesis for compound 16 is shown, note heading, trans-3-(hydroxymethyl)-2-(3-pyrrolidyl) pyrrolidine in column 2 and note, concept of trans stereo-isomer is disclosed. Again, the march textbook, pages 108-111 is relied on to teach the conventionality of Resolution and optical purity. The combination of references is believed to render obvious the claimed compounds.

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Claim 44 is rejected under 35 U.S.C. 102b as being anticipated by Titus et al. and Ninth Collective formula Index Vols. 76-85, Page 4215f.

Specifically, the Titus et al. article deals with thin-Layer Chromatography and the biosynthesis of nicotine and related alkaloids in leaves and the existence of hydroxy-nicotines. The Ninth Collective Formula Index verifies in Page 4215F in column 3, under the heading Pyridine, the 3-(1-methyl-2-pyrrolidinyl), monohydroxy derive in the (S) form which clearly reads on the instant claim.

Claims 45-47 are rejected under 35 U.S.C. 103 as being unpatentable over Titus et al. and March.

The disclosure of Titus et al. has been discussed above as well as the verification in the Formula Index, Ninth Collective Edition for the $C_{10}H_{14}N_2O$ formula. Again, The March text is cited to teach the conventionality of Resolution into Sinister or Rectus absolute configurations and the concept of optical purity raising a presumption of obviousness.

Summary

The C.C.P.A. has taken the position that optical isomers and geometric isomers are unpatentable over each other as well as reacemates absent a

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showing of unexpected results. See In re Norris 84 U.S.P.Q. 458; In re Adamson et al. 125 U.S.P.Q. 233; Brenner et al., V. Ladd, 147 U.S.P.Q. 87 (District Court D.C. 1965)

A prior art statement is required in compliance with 37 CFR 1.97-1.99.

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ALAN L. ROTMAN
EXAMINER
GROUP ART UNIT 121

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